REMARKS

Claims 1-26, 29, 34-36, 41, 42, 45-53, 56 and 57 were pending in the application and were subjected to restriction. (New claims 58 and 59 are now added)

I. The Restriction Requirement

The Examiner has indicated that the claims define ten independent inventions which will not be reiterated in detail below. In brief the inventions have been characterized as:

Group	Claims	Characterization of Invention
I	1-12, 20, 21, 35	modified catalase having a C-terminal PTS1 sequence (S/A/C-K/R/H-L/M), compositions and a use thereof (reducing hydrogen peroxide concentration in cell)
II	13,14	modified catalase having a PTS2 sequence (K/R-L/I/V-X_5-H/Q-A/L/F) at or near N-terminus, compositions and a use thereof
III	15, 16, 22	modified catalase having a PTS2 sequence and a C-terminal PTS1 sequence, compositions and a use thereof
IV	17-19, 56	nucleic acids/host cells encoding modified catalase having C-terminal PTS1 sequence and a use thereof for producing modified catalase polypeptide
V	57	nucleic acids/host cells encoding modified catalase having a PTS2 sequence and a use thereof for producing modified catalase polypeptide
VI	23, 24, 26, 29, 34, 36, 41, 42	peroxisomally-targeted polypeptide comprising modified catalase having C-terminal PTS1 sequence and bound delivery or translocation molecule or moiety and a use thereof (reducing hydrogen peroxide concentration in cell)
VII	25	peroxisomally-targeted polypeptide comprising modified catalase having PTS2 sequence and C-terminal PTS1 sequence and bound delivery or translocation molecule ,and a use thereof
VIII	45-47,49,50, 52, 53	methods of treating disease associated with inadequate levels of peroxisomal catalase using modified catalase (C-terminal PTS1 sequence)
IX	48	methods of treating a disease associated with inadequate levels of peroxisomal catalase using modified catalase having (1) PTS2 sequence at or near N-terminus and (2) a C-terminal PTS1 sequence
X	51	methods of treating or preventing skin wrinkling using modified catalase having C-terminal PTS1 sequence

II. Applicants Response and Discussion of Additional Amendments/New Claims

Applicants provisionally elect, **with traverse,** Group I, which includes claims 1-12, 20, 21 and 35. While claims 41 and 42 were not originally classified into Group I, they are being amended to be dependent from claim 35 which is in Group I, therefore placing them within the scope of the elected invention (as characterized by the Office). The reasons for the traverse are discussed below

Other Amendments and New Claims

Claim 1 is being amended voluntarily in several ways, in part to improve clarity. Note also that the claim now states that the replacement is of SEQ ID NO:1 explicitly in human catalase. Support can be found al least at page 8, lines 27-28 of the specification.

Claim 58 is being added to further indicate that the C-terminal SKL sequence is not preceded by KANL Support for this language can be found at page 9, lines 1-2 (see also preceding paragraph).

New Claim 59 is added to claim the modified polypeptide based on it being specifically encoded by coding nucleotides from a particular reverse primer (SEQ ID NO:18). Support is found at page 37, lines 1 through l 14. The use of SEQ ID NO:18 will result in a modified catalase ending at its C-terminus with KSKL. To further illustrate the encoding, Applicants discuss the way this works in more detail in Appendix A hereto.

III. Office's Reasons for the Restriction and Applicants' Traversal

The inventions listed as Groups I-X allegedly did not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lacked the same or corresponding special technical features. The reasons were as follows.

The Office contends that the only shared technical feature of Groups I-X is that each relates to a modified catalase comprising one (or more) **non-natural** peroxisome targeting sequences. However, the Office further contends that this shared technical feature is not a "special technical feature" as defined by PCT Rule 13.2 as it does not constitute a contribution over the **Sheikh** *et al.* (*PNAS 95*:2961, 1998) (hereinafter "**Sheikh**"). Sheikh was cited for its disclosure of modified catalases comprising a C-terminal PTS1 sequence - SKL (as well as a PTS2 sequence, HRLQWLGHL, immediately following the initial Met). As such, neither the modified catalase fusions nor the PTS1 or PTS2 peptides themselves were considered by the Office to be "special technical features."

An additional basis for restriction was the Office contention that Groups VIII-X (methods) lack unity with Groups I - III (compositions) because Groups I-III already include one method of use of the modified catalase which comprises "unrelated steps" compared to the methods of Groups VIII-X. The Office cites 37 CFR § 1.475 – which does not provide for the inclusion of multiple methods of use with the main invention.

Applicants respectfully disagree with two different aspects of the restriction and the above reasoning.

First, and most importantly, it is noted that the claimed modified catalase polypeptide is distinguishable over that of **Sheikh** for reasons discussed below. **Sheikh** discloses the following (emphasis added):

> "*a nucleotide encoding catalase fused at its C-terminal part to additional nucleotides for the PTS tripeptides SKL (PTS1), and polypeptide corresponding thereof.*"

This is also confirmed in the Material and Methods section (page 2962. left col., paragraph entitled "Generation of Human Catalase Expression Constructs", third sentence)(emphasis added):

> "*This* {referring to primers used} *spans positions -8 to 1,651 of the normal catalase for SKL at the carboxy terminus."*

Claim 1 is directed to a modified human catalase polypeptide in which the native *peroxisomal targeting site* (PTS1), KANL, has been **replaced** by another sequence. That replacement sequence is more broadly claimed as comprising S{A/C}-K{R/H}-L{M}. It is not KANLSKL, the sequence that is described in **Sheikh**. To the contrary, the application expressly and deliberately distinguishes **Sheikh**.

> "*Obviously, then the Sheikh et al. document did not even suggest ...the replacement of the native KANL C-terminus of human catalase with the sequences disclosed herein."*

(page 3, lines 7-9, emphasis added)

> "*Thus, in a preferred modified catalase, the KANL sequence has been removed and substituted with SKL or a functional variant thereof.*"

(page 8, lines 27-28, emphasis added).

Sheikh does not disclose the replacement of the native C-terminal PTS of catalase by another PTS as is defined in claim 1. **Sheikh** discloses a full length native catalase sequence that is fused at its C-terminus to the tripeptide SKL, yielding a C--terminal amino acid sequence over the last 7 residues of KANLSKL. In contrast, the C-terminal three residues in the claimed modified catalase are S{A/C}-K{R/H}-L{M} that have replaced KANL, and with no KANL sequence internal to it. This difference is further emphasized in new claim 58.

Further, **Sheikh's** disclosed PCR primers do not actually encode a catalase fusion product with a C-terminal KANL-SKL sequence at all. Rather, they encode a catalase fusion product with a C-terminal sequence KANL-**L**KL. The relevant PCR primer set forth in the first full paragraph on page 2962 of **Sheikh** is:

5'-TCAGAGTTTTAGCAGATTTGCCTTCTC-3'

The translated terminal 8 residue amino acid sequence when using this primer is EKANLLKL, not EKANLSKL.

The way in which the **Sheikh** reference was applied as a basis for destroying the novelty, of the generic composition claim (and thereby disunifying the invention), does not take into account the foregoing differences. Indeed, when these are taken into account, the Examiner's claim grouping does relate to a single general inventive concept under PCT Rule 13.1, and, under PCT Rule 13.2, and they do possess the same/corresponding special technical feature (modified human catalase at PTS1 as defined above). The modified catalase **is** a special technical feature as defined by PCT Rule 13.2 because it does constitute a contribution over **Sheikh**.

For this reason, the Examiner is respectfully requested to reconsider the Restriction Requirement and withdraw it, at a minimum as to Groups I-VII.

IV. The Restriction Between Group I and the Corresponding Claims of Group VI

Notwithstanding the foregoing, restricting between Group I (modified catalase) and Group VI (modified catalase/delivery or translocation molecule/moiety) is believed to be improper because there would be no serious burden in searching both groups of claims. While the classification of these claims has not been provided, Applicants believe they would be in the same class/subclass. Because the search of such dependent claims to deliverable polypeptides is co-extensive with a search of the underlying modified catalase polypeptide, there is no additional burden on the Office in searching this invention.

For this reason, as well as for the reasons advanced above with regard to the Office's misapplication of the Sheikh reference, the rejoinder, at minimum of Group VI with Group I is respectfully requested.

Since Applicants have provisionally elected Group I, and in view of their position at least as regards rejoinder of the claims of Group VI, Applicants are provisionally withdrawing the claims of Groups II, III, IV, V, VII, VIII and IX (with the exception of claims 41 and 42 as discussed above). The remaining claims of Group VI (claims 23, 24, 26, 29, 34, and 36) are left as active (and tagged as "previously presented") pending the Office's consideration of Applicants' requests. (Applicants understand that if their view regarding Group VI does not prevail, the Office will examine the application treating the Group VI claims as effectively withdrawn.)

V. CONCLUSION

Applicants respectfully requests entry of the foregoing claims as amended, added, and/or withdrawn, and the election of an invention as above, as well as reconsideration of the Restriction Requirement. The claims are now in condition for examination and allowance.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.
Attorneys for Applicant(s)

By /Shmuel Livnat/
Shmuel Livnat
Registration No. 33,949

SL:mak

Telephone No.: (202) 628-5197
Facsimile No.: (202) 737-3528

G:\BN\W\WAYN\TERLECKY1A\(WSU-9)_US\Pto\2008-04-18_Resp_RR_2nd_PAM.doc

APPENDIX A

SEQ ID NO:18 is used in the Examples at page 37. A modified catalase is prepared using SEQ ID NO:18 as a reverse primer. The modified catalase so prepared is broadly described in the Example as "an SKL sequence". Note, however, that the sequence of this reverse primer will result in expression of the modified catalase so that it ends in KSKL (as demonstrated below).

In the table below, the 'steps' from SEQ ID NO:18 to the modified catalase protein are detailed. One must read the "reverse primer" (SEQ ID NO:18) in the 3' to 5' direction, and then translate the complementary transcript. An alignment is also shown with native catalase (row 3) in the corresponding region (using "=" between complementary bases that will hybridize during the process of carrying out the molecular manipulation to "convert" the KANL sequence to KSKL). Wild type catalase amino acid sequences are shown in italics. The stop codon (tga) and subsequent untranslated "codons" are shown in bold with the nt's in lower case. In the amino acid sequence of the fifth row (AA encoded by 3'-5' complement), the "place" of the stop codon is shown as an "*" and the subsequent 4 "encoded" amino acids KLAP following the "|" that are not made due to the stop codon are indicated in a lighter gray font.

SEQ ID NO:18	5'-GGG CGC AAG CTT TCA CAG TTT CGA TTT CTC CCT TGC CGC CAA GT-3'
Reverse -3'-5' *(Catalase wt)*	3'- GT AAC CGC CGT TCC CTC TTT AGC TTT GAC ACT TTC GAA CGC GGG-5' = === === === === === == = == === === *AC TTG GCG GCA AGG GAG AAG GCA AAT CTG TGA*
3'-5'Complement	3'- CA TTG GCG GCA AGG GAG AAA TCG AAA CTG **tga|aag ctt gcg ccc**-3'
AA encoded by 3'-5'Complement	L A A R E K S K L * | K L A P **Stop |**
(Catalase wt AA) (nucleotide)	*L A A R E* ***K A N L*** *** *AC TTG GCG GCA AGG GAG AAG GCA AAT CTG TGA*